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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/651,305	08/28/2003	Chia-Gee Wang	U 014775-5	9020

140	7590	04/15/2010
LADAS & PARRY LLP 26 WEST 61ST STREET NEW YORK, NY 10023		

EXAMINER	
POLANSKY, GREGG	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
04/15/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

Office Action Summary	Application No. 10/651,305	Applicant(s) WANG, CHIA-GEE	
	Examiner GREGG POLANSKY	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 December 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12, 14-24, 26-47, 49-59, 61-97 and 99 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 5, 7, 12, 16-24, 26-36, 38, 40, 42, 47, 51-59, 61-65, 67, 69, 71, 76-88, 90, 92, 97 and 99 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2,4,6,8-11,14,15,37,39,41,43-46,49,50,66,68,70,72-75,89,91 and 93-96.

DETAILED ACTION

Status of Claims

1. Applicant's response, filed 12/10/2009, to the Office Action mailed 8/18/2009 is acknowledged.
2. Claims 1, 3, 5, 7, 12, 16-24, 26-36, 38, 40, 42, 47, 51-59, 61-65, 67, 69, 71, 76-88, 90, 92, 97, and 99 are presently under consideration.
3. Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. Claims 1, 3, 5, 7, 12, 16-24, 26-36, 38, 40, 42, 47, 51-59, 61-65, 67, 69, 71, 76-88, 90, 92, 97, and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mills (U.S. Patent No. 6,224,848), in view of Wang (U.S. Patent No. 5,627,871).

Mills teaches, *inter alia*, a method for eliciting tissue necrosis in treating cancer, by administering a compound (*e.g.*, cisplatin) that binds to targeted tissue DNA, wherein said compound comprises an atom (*e.g.*, platinum) that is excitable with radiation in a distinct narrow frequency band and energy level, causing an Auger electron cascade resulting in radiolysis of DNA. See Abstract and columns 108-110, claims 1, 5, and 9). Note that the compound, cis-diamminedichloroplatinum (II), taught by Mills in column 109, line 8, is the chemical name of cisplatin. Since cisplatin taught in the reference is the same as cisplatin recited by the instant invention, the properties of the elected compound (cisplatin) recited by the instant claims would also be encompassed by the cisplatin taught by Mills. For instance, the rate of physiological excretion of cisplatin and stability against dissociation of platinum from cisplatin during the time prior to complete excretion of cisplatin (*e.g.*, instant Claims 16 and 17 respectively) would be identical in both the reference and the instant invention. Similarly, the K- and L-absorption edge of platinum and the amount of Auger electrons released from the platinum in cisplatin and their effective range would be identical in the Mills reference and the instant claims.

The instant invention differs from the cited reference in that the cited reference does not teach the Applicant's preferred method of eliciting Auger electron cascade (*i.e.*, using line emission x-rays) from the selected element (*i.e.*, platinum). However, the secondary reference, Wang, teaches the preferred line emission x-rays to be well

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known in the art. See column 10, lines 27-51. Wang teaches an end window transmission x-ray tube possessing a metal foil target on said end window, the thickness and composition of the metal foil target and the e-beam energy focused thereupon generate a micro-focused bright line x-ray beam of pre-selected energy. See Abstract.

Therefore, one skilled the art would have understood that the substitution of one monochromatic energy source (which causes an Auger electron cascade in the target metal, *e.g.*, platinum in cisplatin) for another monochromatic energy source capable of producing an Auger electron cascade in the metal. It would have been obvious to the artisan to use the x-ray source taught by Wang because of the increased convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills.

The references do not teach the treatment of cells removed from and returned/transplanted back to a mammal. The references do not teach a kit comprising an x-ray tube having a target comprising a selected metal, and a compound (cisplatin) comprising a selected element (Pt).

One skilled in the art would have well versed in the practice of removing bone marrow and various other cells from the body for treating certain cancers (*e.g.*, x-ray treatment) and returning/transplanting these cell back into the body. It would have been obvious to use the methods taught by Mills and modified by the teachings of Wang to seek an improved cancer therapy. It would also have been obvious to said artisan to “package” the essential components necessary to practice these methods. One would

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have been motivated to do so to provide a more convenient and efficient means for practicing a method of cancer therapeutics.

6. Applicant asserts the instant claims are drawn to “a step of irradiating a selected region, in which malfunctioning cells comprising a compound with the selected element associated with DNA of the malfunctioning cells are located, with line emission x-rays so as to cause emission of Auger electrons in a dose of at least 10^6 Gy *in situ* within a few atomic distances from the selected element whereby to localize the effects of disrupting DNA to the malfunctioning cells [and] this feature of the claimed method was not predictable to one of ordinary skill in the art from the cited references and the references could not provide even a reasonable expectation of success for the invention as claimed.” Applicant argues “[o]ne of ordinary skill in the art could not have predicted from the cited art that the substitution of the claimed line emission X-rays for the gamma-rays of Mills would produce and achieve the claimed results.” Further, Applicant argues “[t]here is nothing in Mills that would show or suggest if or how the method described therein could be modified to create an Auger cascade other than by Mossbauer absorption using gamma rays of a corresponding Mossbauer absorption frequency.”

The Examiner respectfully disagrees. As previously discussed, Mills teaches the Auger electron cascade is responsible for the therapeutic (*i.e.*, anti-tumor) effects of the disclosed method. One of ordinary skill would have recognized that an Auger electron cascade can be precipitated by means other than described by Mills (e.g., x-rays instead of gamma-rays). Wang teaches an Auger electron cascade precipitated by an

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x-ray source which reads on the x-ray source of the instant claims. Further, as discussed above, the method of eliciting an Auger electron cascade using x-rays taught by Wang offers improved convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills. The K- and L-absorption edge of platinum and the amount of Auger electrons released from the platinum in cisplatin and their effective range would be identical in the Mills reference and the instant claims.

The method of Cash et al. (cited in Applicant's arguments) does not rely on the release of Auger electrons for its therapeutic effects, but rather on the use of a contrast agent to stop more x-ray photons in the tumor than the amount stopped in the absence of contrast agent in healthy tissue.

Applicant argues "Wang does not show or suggest the use of line emission x-rays tuned to the K- or L- absorption edge of a selected element to create an Auger cascade that can be used selectively to destroy tumor cells **without destroying healthy tissue.**" (Emphasis by Applicant)

As discussed above, the skilled artisan would have been motivated to use the x-ray source taught by Wang to stimulate an Auger electron cascade because of the improved convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills.

Conclusion

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7. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected.

8. No claims are allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614